

CA3 ONHW Q90
82 U6504 v.5

Pamphlet
box

URBAN/MUNICIPAL

Report of the Mount
Sinai Medical Center on
the Upper Ottawa Street
Landfill site.
Reference 37

CA3 ONHW Q9D
82 46504 V.5

Ref. 37



THE MOUNT SINAI MEDICAL CENTER

ONE GUSTAVE L. LEVY PLACE • NEW YORK, N.Y. 10029



Mount Sinai School of Medicine • The Mount Sinai Hospital

Philip J. Landrigan, M.D., M.Sc.
Director, Division of Environmental
and Occupational Medicine
Department of Community Medicine

October 23, 1985

(212) 650-6173

Ms. Anne Koven, Research Director
Upper Ottawa Street Landfill Site Study
20 Jackson Street West, Suite 412
Hamilton, Ontario L8P 1L2
CANADA

Dear Ms. Koven:

Thank you very much for having sent me the report from the Upper Ottawa Street Landfill Site describing the residents' health study. I was pleased to have had the opportunity to review this document.

This report describes the results of a morbidity study which was conducted of residents living near the Upper Ottawa Street Landfill Site in Hamilton. You compared the self-reported health histories of persons living within 750 meters of the landfill site with those of persons living at greater distances. Also, you distinguished between persons who had lived near the landfill in the years 1976 to 1980, when dumping was most intense, and persons who moved into the area subsequent to 1980. As a comparison group, you included persons from a population of approximately similar socioeconomic status living elsewhere in the City of Hamilton, approximately five miles from the landfill site.

The objectives of your study were (1) to determine whether incidence rates of certain illnesses were higher in persons living near the landfill than in the control group and (2) to determine whether any cause and affect relationships existed between illnesses reported in landfill residents and toxins emanating from the landfill.

On the basis of a previous study which you had conducted of workers employed on the landfill site, you determined in advance of this study that the following health conditions were of greatest concern: respiratory problems, dermatologic problems, narcotic syndromes, and mood disorders. Quite reasonably, then, you established these conditions as your prior hypotheses.

Your survey was undertaken through face-to-face interviews. These interviews were conducted by trained interviewers from a survey research firm. The primary targets of your interviews were female heads of household. A standardized questionnaire was administered to these persons. This questionnaire sought information on the health conditions which had been established as prior hypotheses, as well as information on other health conditions and on demographic and social factors. Where appropriate, you went to the medical records of study subjects and abstracted relevant information.

Your response rates for households currently living adjacent to the landfill site ranged from 80 to 84 percent. Among families who had moved away from the landfill site, your response rate was 75%. In the control population your response rate was 67.8%. You found that the families living near the landfill site had somewhat lower socioeconomic status, lower educational attainment and lower income than the control families. There was no evidence, however, that sicker persons had been attracted to neighborhoods close to the landfill site.

The analyses of the data on adults showed positive associations between residence adjacent to the landfill and four classes of symptoms: respiratory, skin, narcotic and mood symptoms. Relative risks for the occurrence of each of these classes of symptoms in persons living adjacent to the landfill as compared to the controls ranged from 1.5 to 2.5, and each of these associations had a statistical significance of less than 0.01. Further, statistically significant gradients were observed in relation to proximity to the landfill for each of these four categories of symptoms, and gradients were also observed with regard to duration of residence near the landfill. Of particular interest was the observation that skin symptoms were associated with recreational activities on or about the landfill. It was observed that persons who had moved into the neighborhood near the landfill since 1980 had increased instance of narcotic and mood symptoms as compared to controls, but that these persons had no increased incidence of either respiratory or skin complaints.

In the analysis of the pediatric data, positive associations were observed between landfill site exposure and skin, narcotic and mood symptoms. Respiratory conditions were less strongly associated with proximity in children than they were in adults. Gradients with proximity and with duration of residence were not so clearly defined in children as in adults, but among children who had been long-term residents in neighborhoods near the landfill, proximity gradients were evident for respiratory, skin and mood symptoms. As in adults, skin symptoms were found to be associated with recreational activities on or about the landfill. There was no evidence that less healthy children had been attracted to residence in the neighborhoods near the landfill site.

October 23, 1985

The analysis of pregnancy is based on data from 981 pregnancies, 386 of them in exposed women. No differences were seen between exposed and control women in terms of pregnancy risk factors, including medical factors or exposures to medications. No statistically significant differences were seen between the exposed and control groups in the distribution of live births, stillbirths, miscarriages or abortions. No unique or unusual pattern of birth defects was noted, and no increase in total birth defects was seen. The authors carefully point out the limitations of statistical power which are imposed on all of these analyses by the relatively small number of pregnancies available for study.

In the discussion, the authors link their manifold findings by relating them to a modified listing of the criteria for causality which were established by Bradford Hill and refined by Sackett. In summary, the authors concluded that strong, statistically significant associations existed in adults between residence near the landfill and the occurrence of certain narcotic, mood, skin and respiratory conditions. These findings were consistent with the results of the workers' study conducted previously. Symptoms were more common in persons living close to the landfill than in those at a distance, and more common in persons who had lived there a longer duration of time than in shorter term residents. Among children, strong associations were seen between residence adjacent to the landfill and narcotic, skin and mood symptoms as well as itchy eyes.

The authors go on to state that these constellations of symptoms could be related either to materials emanating from the landfill or to a heightened perception of exposure with a resultant increased tendency on the part of residents to identify and report their perceived health problems.

The authors conclude that their data do not permit the drawing of a distinction between these two possible etiologic explanations. Cautiously, they point out that their conclusions must be evaluated in the light of three weaknesses in their data: 1) the high refusal rate among their control population, 2) differences in socioeconomic status between exposed and control populations and 3) the lack of precise definition of the symptoms under study.

Evaluation. I found this study to be of high quality. The authors were engaged in a difficult exercise and they coped very well with the problems with which they were faced.

The questions under investigation are clearly stated in the introduction. The presentation of the background is clear. The notion of using the results of the workers' study as a hypothesis-generating exercise and guide for the present study is a very ingenious and quite proper approach. The workers, as the authors note, would be expected to have heavier exposure to any materials in the landfill than adjacent residents. Therefore, any illnesses

observed in workers should provide a reliable, high-dose guide to the problems to be anticipated in residents. The review of the literature on pages 15-19 is quite elegant. The authors note correctly that an ideal study of health effects in persons residing near a landfill should be based on careful measurement of environmental exposures. They go on, however, to note that in a pragmatic world, which abounds in chemical mixtures, such precise measurements are seldom available and that therefore such surrogate indicators of exposure as duration of residence and proximity of residence must be used in lieu of precise chemical data.

In the methods section, the authors describe very clearly the assumptions and the decisions which they made in order to rationalize their use of surrogate exposure indicators. I found this discussion to be clear, straightforward and reasonable. I wish that precise chemical data were available and I am somewhat surprised that at least some chemical data were not available. However, I cannot fault the authors on the approach which they have taken here.

The control population appeared to have been reasonably sought. It is unfortunate that differences in income and in socioeconomic status crept in between the exposed and control populations, but overall the match between the exposed and control was acceptable. Also, I noted the authors' statement that no more appropriate population was available elsewhere in Hamilton.

All of the issues surrounding the questionnaire appear to have been very thoroughly considered. The questionnaire itself was carefully developed and was based in part upon questionnaires used previously, such as the Canada Health Survey. I was pleased to note that the interviewers were blind to the hypothesis being tested and were unaware of which questionnaire items were distractors. The procedure of using multiple call backs is highly laudible, and the high response rate obtained attests to the persistence of the interviewers.

In regard to data analysis, I have little to add. The procedures used were state-of-the-art. The investigators made ingenious use of their various study groups to evaluate issues of bias, and I have no adverse criticism to make of those procedures.

Finally, I consider that the conclusions which the authors drew are reasonable. After reading and rereading the report I share their frustration at being unable to decide whether the symptoms resulted from actual exposure to toxins emanating from the landfill or from an altered emotional state. I am tempted to speculate that the respiratory and skin symptoms are the more likely to

October 23, 1985

have resulted from actual exposures to toxins. I base that speculation on the observation of an increased frequency of skin symptoms in persons who had recreational exposure to the landfill as well as on the observation (Table 18) that skin and respiratory symptoms were not elevated in short term residents whose mood and narcotic symptoms were elevated. However, I have no firm basis for making that distinction, and at the end I must concur with the cautious interpretation of the authors.

I agree with the conclusion reached at the bottom of page 150 that for the purposes of future policy decisions the workers' study will be declared positive with respect to the high and moderate credibility hypothesis. That conclusion, quite properly, is based on the consistency of results between the worker and resident studies.


Recommendations for future studies. In my opinion, it will be reasonable in the future to monitor the occurrence of skin, respiratory and neurologic symptoms both in landfill site workers as well as in persons who may continue to reside near the landfill. This monitoring ought to be most intense among the workers, since their exposures will likely be the heaviest.

Monitoring of skin symptoms can most efficiently be accomplished by simple questionnaire. Pulmonary symptoms can be monitored by questionnaire and possibly by occasional (every three to five years) chest X-ray and/or pulmonary function studies. Neurologic symptoms, such as narcotic or mood symptoms, can best be analyzed by questionnaire; specific neurologic follow-up studies would, however, be indicated if any evidence of neurologic abnormalities developed.

Finally, I am impressed by the association between recreational activity on the landfill and the occurrence of skin symptoms. In light of that observation, I should think it would be wise public policy to recommend that the area near the landfill be closed to all recreational activity.

I hope that these comments are helpful. Please do not hesitate to call upon me if I may assist you further.

Sincerely,


Philip J. Landrigan, M.D.
Professor

PJL:jlr
Enc.



File.

The University of Alabama at Birmingham
School of Public Health
Department of Epidemiology

Philip Cole, MD, DrPH
Professor and Chairman
205/934-6707

November 18, 1985

Ms. Anne Koven
Upper Ottawa Street
Landfill Site Study
20 Jackson Street West
Suite 412
Hamilton, Ontario L8P 1L2
Canada

Dear Ms. Koven,

Enclosed is my report on the Upper Ottawa Street Landfill Site Study. I apologize for its tardiness, but a number of circumstances precluded my completing it sooner.

You asked in your letter of September 30 if I would comment on certain ideas. I offer you the following:

I see no point in attempting any follow-up clinical investigations at this time. I interpret the Residents' study as essentially negative or at most only faintly suggestive of some effect. Given the resources that have already been expended on what is certainly a non-problem or a trivial problem, I could hardly support the position that further work should be done.

The same interpretation also suggests to me that it would be unnecessary and unwise to expend any resources monitoring the health of residents in the vicinity of the landfill. The proposed spirometry, neurobehavioral testing and cancer registry appear to me to be entirely uncalled for. I can only wonder how negative the Residents' study would have to have been in order that such propositions would not even be mentioned. Certainly this study did not have to be done in order to make a judgement about a cancer registry; the study is completely irrelevant to that issue.

Sincerely yours,

A handwritten signature in cursive script that reads 'Philip Cole'.

Philip Cole, M.D., Dr.P.H.
Professor and Chairman

PC/vcg

Encls.

TITLE: Residents' Health Study Report for the Upper Ottawa
Street Landfill Site Study

AUTHORS: C. Hertzman et al

REVIEWER: P. Cole

DATE: 18 November 1985

This report describes the background, methods, findings and interpretation of what is, essentially, a prevalence survey of various groups of people selected for their proximity to or distance from a large active dumpface. The study followed a study of the health of workers at the same dump but failed to make maximum use of that study because of time pressures. The present study, by virtue of its size, duration and mode of data gathering (as well as other considerations) appears to have been adequately funded despite internal disclaimers of this.

Despite the various strengths and resources available, not the least of which is the interdisciplinary background of the authors, the final report suffers from a series of limitations and is singularly lacking in persuasiveness. This is so despite its length and the presentation of superfluous details including trivia. Further, at many points the report evidences a lack of philosophical and scientific expertise, such that this reviewer can feel comfortable with no interpretation of the data other than: This study provides no persuasive evidence that the Upper Ottawa Street Landfill ever produced any disease or symptoms. However, a strength of the report is that it prominently mentions and attempts to deal with most of the limitations of the research (e.g. pointing out the poor response of controls, their relative stability and the high smoking levels of the exposed).

Consider the interpretation and explanations offered on pp. i, ii and repeated on p. 149. Note the allusion to "causative agent" (p. i, line 6 from bottom) apparently referring to putative cause(s) of disease or symptoms. But, in the very next line the word "causes" is used to allude...to what? Apparently to reasons for a non-persuasive positive study. As is evident, the following "cause" number two is not a cause (except of unimpressive results) and is universally termed "bias". Perhaps the authors just could not bring themselves to use the term bias in describing the results of their own study.

To the extent that the study is represented by its authors as one that is weakly positive for a few subjective symptoms and that even these results may very well be due to bias few will quarrel with it. But, if the study is used to defend the idea that the landfill caused disease it will be attacked.

I list below a few points that I noted and that might be considered in any revision of the report.

General - The report is too long. Virtually all of the background could be eliminated and the most relevant material included in the discussion. The methods would better focus on what was done. Details of what was not done (e.g. mail questionnaire) and of how people were trained belong in an appendix. Information on response rates and follow-up rates of movers should be dealt with more prominently. Eliminate repetition and verbosity; this report includes nothing that need be stated twice except for what is to be included in the summary.

Page 1, line 6 from bottom: substitute "different" for greater. Current phraseology here and elsewhere suggests that authors had a bias in favor of positive results.

Page 2, objective 3 appears never to be mentioned again, nor did the study deal with it. Suggest delete.

Page 3, line 3 in paragraph 2. "...as much as..." means "five or less, including zero." Can you be more specific? What seems a reasonable average?

Page 8, line 5. susceptible is almost certainly the wrong word.

Page 8, point 2. I shall not go into it here but I (and others) have argued elsewhere that this is not the multiple comparisons problem. There is no need to correct downward your criterion of statistical significance. But then again, the whole report would be improved if it gave more attention to results and less to the statistical significance (or lack thereof) of results.

Page 9, last lines. What exactly does this mean? Just how relevant is the workers study to this one. If only at the interpretative stage drop all reference to it until the discussion.

Table 1. Give data and results instead of + and - signs wherever possible.

Page 20. Distance criteria are not mutually exclusive. In what category were placed the households at 500m?

Page 30. The expression "female head of household" in the USA means a household with no man present. You seem to imply something else. Canadian usage?

Page 41, line 4 under (b). Jargon.

Page 42. Expression $p(RR)$ is unique to this report. Suggest you eliminate it.

Page 51, line 4. Recall unlikely? I say very likely.

Page 52, lines 4-6. A major limitation of the study.

Page 60, lines 16-17. Not significant! Evidence? The authors of this report apparently believe that significance testing is a useful approach to potential confounders. Apparently, they have the view that a variable that does not differ significantly between groups cannot confound. This is wrong.

Page 150, line 5. Suggest "follow-up period" in place of "latent interval". Perhaps there is nothing "latent".

Page 39-40. I do not understand this. It appears to be neither a measure of risk (which does not include person-years) nor rate (which is instantaneous not cumulative). Actually, the measure appears to be a rate and the word cumulative seems to imply "over the whole period of residence" or similar.

Subject: Upper Ottawa Street
Landfill Site Study
(Residents' Health Study)

General comments:

1. This study appears to be well thought out and carefully done. Attention has been paid to problems of bias, misreporting, and migration, as well as the usual confounders of age, sex, socio-economic status, etc.

2. Because much of the manuscript describes the attempts to avoid or minimize or measure biases and confounding, I lost the thread of the arguments in the early reading -- and I found it necessary to go over the material more than once. I was confused (and lost) by the tables relating to the bias considerations (pp. 42-44), and it was not until I got into the various pieces of the results section that these ideas began to clarify. (The words "conservative" bias and "non-conservative" bias need to be replaced by something more descriptive.)

3. The presentation toward the end of the manuscript (Tables 67 and 69) was particularly helpful. As I read the manuscript I found myself asking for a summary table (or tables) which would include the following:

- Table: a) Name and number
b) Reason for inclusion (i.e., What idea or concept was being examined? What was this table expected to show or evaluate?)
c) What did the table show?

This was largely accomplished by Tables 67 and 69 -- although they contained so much information that it was necessary for you to use symbols and abbreviations, which, unfortunately, were sometimes different for different columns. Breaking these tables up or presenting the material in question/answer form might help.

4. For several tables I found myself computing means, or medians, or percentages (some of which were then given in the text). I find that looking at these specific measures helps me understand the data far better than looking at chi squares or p values. Some of the tables on which I noted such computations were numbers 10, 11 (and Figure 4), 12, 13, 14, 46, 52, 53, 54, 55, 57, 62, 63, 64, 65.

5. The handling of the probability levels (by dividing the nominal probability for "significance" by the number of comparisons made) is a very conservative approach. If there were any positive correlations among the various comparisons, this would reduce the "threshold" probability for triggering statistical significance too much to be a literally correct statement of the probability. However, it seems to me that this over-conservative approach may be appropriate. Perhaps a review should be made to see what comparisons might have been called significant, had a less conservative approach been taken, to see if some pattern or clustering appears.

6. Develop all the data, and present them separately, showing whether the landfill appears to be secure now (or not).

7. It is unfortunate that despite the reasonable attempts at neighborhood matching the controls turned out to be rather different than the residents in several ways. In general, it appears to me that the problems this generated were rather well handled -- although I wondered whether some of the log-likelihood, or logistic regression techniques might serve to handle the confounders somewhat better. I have no suggestions re volunteer/non-volunteer response (rate) bias.

More specific comments re results:

Table 10: I would like to see medians, rather than mode -- although this would in no way alter the conclusions. (Income, family sizes)

Figure 5: Because of the wide groupings, this doesn't provide much information. Do you need to show this -- or should you show children born (or conceived) while mother was resident?

Table 12: Smoking: In addition to the comparisons given, isn't sex an important discriminator?

Table 13: The age data do not seem consistent with the % smokers. Generally the higher % smokers, the lower the median age commenced smoking. Not here.

	% smokers	median age started
Exposed	39.9	17.5
Controls	26.8	17.8
Movers	40.2	18.2
Recent	35.2	17.6

Do sex differences confound these data?

Table 18: I find the inversions with distance hard to understand in view of the elevated levels compared to controls. (You say this too, on p. 71.)

Tables 20, 34, 35, 41, etc.: I am impressed that in several places the "Movers" show the greatest mood effects -- perhaps one of the factors that led them to move. (See also p. 81, bottom.)

p. 74 (d): (Trivial language suggestion)
line 8 - I suggest the word "difference" rather than "increase."

(e): Could the probabilities be combined -- e.g., in the manner suggested by R. A. Fisher (and/or lots of other people)?

p. 83 (1): As noted later, there is very little cancer (of any kind) anticipated in so young a population. The statistical power of the data here to uncover (say) a 2-fold increase should probably be reported.

Table 28: The lack of independence among many of these conditions needs to be more strongly emphasized. (These are not really 25 different conditions.) You talk about this on p. 88. I would be curious to know what these items (loss of appetite, etc.) showed for movers vs. non-movers.

Table 45: Does the footnote mean to say ". . .terminated during or after. . .?"

Pregnancy-termination tables: It was not clear to me that possible age-of-mother effects were taken into account. (Did I miss this?) Diabetes in controls?

These findings of no deleterious effect are extremely important.

Table 52: The % adverse outcomes (for all groups) seems high. Have you other comparison data?

p. 113 - Medical Chart Abstraction Study: This section is both a methodology section and a results section. It might answer some of the questions about adequacy (and accuracy) of reporting if it came earlier.

I had some trouble understanding this section, particularly the discussion of confirmation, or possible confirmation of unreported conditions.

p. 113 top: I would suggest that not only was there an attempt to assess whether there were continuing health problems, but also an attempt to see if there appeared any new, chronic illnesses with long expression times, or latent periods. One of those might be the "bones and joints" problems mentioned on p. 135 and Table 66. (My note on Table 66 says "More needs to be made of this" -- but what more I had in mind when I first read it I no longer know.)

Discussion: If the summary tables suggested above are constructed, it may be possible to build the discussion around them -- which might help sharpen the conclusions. (As indicated earlier, I had troubles with Table 67 -- in keeping all the information straight.) Perhaps a summary column "Is it real" (answers: Yes, likely, not likely, no) might be added to Table 67.

Two summary tables, perhaps:

1. These we think are real effects.
2. These we think are not.

Summary:

I am impressed by the care taken in this study to provide a balanced review of the potential problems, and to reduce, or at least to account for the several kinds of bias that studies of this type are subject to.

Because of the length and complexity of the report there is a need for an executive summary emphasizing the findings (both positive and negative) and having a short description of the attempts to minimize or measure bias. The present summary may be somewhat too short -- I would be tempted to write the caveat sentence, near the bottom of page i, as a statement of fact, i.e.:

"Specific causative agent(s) have not been identified. At least two possibilities exist:

1. A combination of vapors . . ." etc.

Following possibility number 2, I would add my best judgment appraisal -- derived from my "These are real," "These are not real" tables.

Concerning the possibility for further work, if some semi-automatic inexpensive registry system could be devised, I would want to follow up on "bones and joints," and cancer incidence. If techniques improve (and results become more interpretable) and become less expensive, I would want to see some periodic immune surveillance procedures put in place.

Marvin A. Schneiderman, Ph.D.

"RESIDENTS' HEALTH STUDY REPORT
for the
UPPER OTTAWA STREET LANDFILL STUDY"

-- A REVIEW BY
S.D.WALTER

Department of Clinical Epidemiology and Biostatistics,
McMaster University, Hamilton, Ontario.

October 22, 1985.

1. INTRODUCTION

This review has been prepared in response to a letter dated September 30, 1985, from Anne Koven, Research Director of the Upper Ottawa Street Landfill Site Study. I had previously acted as an external reviewer for the report on the health study of workers at the landfill site. As before, I will concentrate in my review on the design and analytic methodology employed in the study, as described in the "Residents' Health Study Report" (hereinafter referred to as the Report).

Particular emphasis will be put on the quality of evidence offered for or against the various health effects being investigated, taking into account the fact that the study took place after the period of presumed exposures near the landfill. Because of the considerable public concern which has been raised, a major issue in the interpretation of the residents' study is whether the investigators have managed to adequately deal with the problems of recall bias on the part of study participants, especially those living near the landfill.

Another key issue in this study is the use of a control region away from the landfill; data gathered in this area were used to assess the "normal" rates of the various disorders and symptoms under investigation. A valid comparison of the landfill-exposed and control regions requires that the effects of other important variables (confounders) have been eliminated, either by the design at the sampling stage, or during the statistical analysis. I will also emphasise this point in my review.

A further issue raised by Anne Koven is the feasibility of further follow-up work, such as the development of a registry to monitor the health of this population in the future. I will deal with this issue in section 3

of my review. In section 2 of this review, I will make a number of specific points on the study, dealing with issues in approximately the same order as they are discussed in the Report. Then in section 3, I will draw some general conclusions.

2. SPECIFIC POINTS

1. Relationship of results of worker and residents studies.(Page 8 of the Report).

It had previously been decided that a study of the workers at the landfill site should precede the study of nearby residents. The rationale for this was the workers would constitute a high dose exposure group, and might "be particularly susceptible to any potential health impact associated with exposure to the landfill". It is probably true that workers had a higher average exposure on a per hour basis than did the residents; however it should be borne in mind that at least some of the residents may actually have had greater cumulative exposure than the workers, by virtue of their being exposed for more hours of the day over several years. It is also possible that chronic exposure of residents at a lower level is more significant in its impact on health than intermittent exposure at a higher level during working hours for the landfill employees.

While I think the Committee and the Advisory Health Group were correct in their decision to study the workers first, we should not rely overmuch on the consistency of results between the worker and resident studies in order to infer causal effects on health due to landfill exposure. As the investigators have said in some detail, there is great uncertainty concerning the nature of the exposure in terms of its chemical composition and the dose level to specific individuals in the nearby community or in the

landfill workforce. Vague or missing exposure information is typical of many environmental investigations of this kind, and this fact weakens the ability of any study to show causal health effects through the usual criteria as adopted by the investigators. As a result, data from this study are open to a wider range of possible interpretations than would have existed with perfect exposure data.

Another factor to be considered in the worker-resident comparison is the "healthy worker" effect. It is well known among epidemiologists that groups of persons who are employed tend to have better health, on average, than the general population. If this phenomenon applied to the worker and resident groups studied here, it would tend to cancel out any effect due to the higher exposure levels of the workers, at least inasmuch as such effects would be assessed by the absolute incidence rates of disorders and symptoms. Fortunately, the investigators have relied almost always on relative comparisons of rates within the worker groups and within resident groups. As long as the healthy worker effect may have acted to reduce the rates of reporting of all health abnormalities in the worker groups in the same relative proportions, it will not have biased the worker-resident comparisons of associations with exposure. On the other hand, if the healthy worker effect is greater for some disorders and symptoms than for others, then the pattern of significant associations with landfill exposure would not be the same. Although there is no direct evidence on this point in the Report, other studies have shown that the healthy worker effect indeed does vary by factors such as the duration of employment, age, sex, and type of disease under investigation.

The investigators in this study have done well to specify their rules for determining causality. However the uncertain exposure information

inevitably reduces the certainty of their conclusions, either positive or negative. Also as discussed above, it is perhaps too demanding of the data to require consistency between the worker and residents studies in order to show causality.

2. Nature and intensity of exposure (Page 9).

It is stated that the nature and intensity of exposures to residents could not be reliably estimated. This is disappointing in itself, but perhaps the investigators might have said in more detail what efforts were made to construct such estimates. If this situation is typical of others which will be studied in the future, the hydrologists, toxicologists and other related scientists would have had much to learn from the experience gained here, despite their ultimate failure.

3. Definition of residents exposure distance groups. (Pages 20-21)

Much of the analysis concerns various comparisons of persons living "very near" or "near" the landfill. These groups are defined as having a residence 250-500 metres or 500-750 metres from the landfill, respectively. The Report states that this division was to some extent arbitrary, and was determined mainly from consideration of sample size and cost. The analytic comparisons are then on a group level, ignoring the specific distances of each household from the landfill.

Given that the distance of each relevant household must have been determined rather precisely, an alternative analytic strategy would have been to use the "distance from landfill" as a continuous exposure variable, rather than the relatively crude distance grouping actually adopted. It is likely that such an approach would have had greater statistical power to show adverse health effect of landfill exposure, by taking the detailed "exposure distance" into account.

The continuous distance measure would also have been better suited to test the dose-response aspects of exposure. Dose-response is considered in the Report by comparisons of the 250-500 m., 500-750 m. and control regions, thus effectively limiting this part of the analysis to three exposure categories. This method will therefore have limited power to demonstrate the dose-response, and even less power to demonstrate non-linearity (as discussed in my point 17 below).

4. Adequacy of distance from landfill as a measure of exposure.

It is obvious that distance of residence from the landfill does not completely represent the effect of exposure. The investigators did also question about recreational activities near the landfill, but there are undoubtedly many other factors which would influence a given individual's exposure pattern over time. Residences at the same distance from the landfill do not necessarily have the same exposure levels, because of variation in the wind pattern over the study region. Individual exposure levels will also vary because of differences in the amount of time spent at home (e.g. homemakers vs. persons working away from the house) and the amount of time spent outdoors at home.

Apparently the investigators have made little attempt to control for such factors in their analysis. At the least, these other variables will have acted to reduce the efficiency of the statistical analysis used in the Report, and at worst will have acted to bias the conclusions. If, for example, the proportion of persons working away from the home is the same at various distances from the landfill, then no confounding exists and the only loss will be one of efficiency in the analysis. On the other hand, if the various parts of the study region differ in their social make-up so that the proportion of persons working away from home does vary, then this factor will potentially confound the comparison of groups of persons living at

different distances from the landfill. Depending on the direction of the social gradient, such confounding could either have spuriously enhanced an apparent effect of landfill exposure, or have reduced the effect below the level which would have been observed by taking the confounding variable into account.

It is disappointing that the investigators did not attempt to deal with this issue. Given their obvious concern with the limited exposure data available from the toxicologists, one might have hoped for very tight control of "pseudo-exposure" variables which include distance of residence from the landfill, but which could also have included other aspects of individual lifestyles, as suggested above. In their defence, the reliable assessment of such lifestyle variables might have been difficult, given the public concern about the landfill which existed before the study took place. There might very well have been a tendency of persons near the landfill to over-report the amount of time they spent at home or otherwise near the site.

5. Mailout vs. personal interviews. (Page 23)

The Report states without elaboration that mailout questionnaires "proved unsatisfactory". While I would generally prefer data from a personal interview (if this is feasible within the budget), it would have been interesting to know how, specifically, the mailout was unsatisfactory. If, for instance, there were difficulties with question comprehension in the mail version of the questionnaire, could the same difficulties have persisted (maybe at a lower level) in the personal interviews? How was the personal interview schedule modified in light of the experience with mailouts?

6. Household selection from tax assessment rolls (Page 26)

The investigators were careful in their attention to the way in which

the population evolved over time, at least as indicated by the assessment rolls.

In the ideal world, one would like to sample from all persons resident in the area. The assessment rolls probably represent a close approximation to this ideal, but the investigators say little about who might or might not be listed on these rolls. For instance, would short-term tenants be likely to have been missed? Also, it is troublesome to read that there is some double reporting of some families; such double reporting may mean that some families are more likely to be selected into the sample than others, unless specific provision for double listings (multiple listings in general) is included in the sampling protocol. Were such provisions made, and what causes families to be double listed in the first place? I expect that one can not do much better than use the assessment rolls sampling method, but it would still be useful to hear about some of these potential problems.

7. Matching of control community (page 29 and onward).

The ideal control community would be one that was identical to the landfill-exposed areas in all respects except exposure. In practical terms, one attempts to choose a region which matches as closely as possible with respect to known covariates which may affect or be associated with disease status. This is clearly one of the most crucial aspects of the design of this study.

Unfortunately it appears that the ideal matching community did not exist, at least within Hamilton. As discussed below (see also point 15) I have some concerns that important differences exist between the exposed and control communities, and these may not have been adequately controlled in the data analysis.

The criteria by which the Gilkson neighbourhood was chosen are not well specified, beyond a statement that it was the "closest community match" in

Hamilton. It appears (page 29) that the choice may have been made entirely on the basis of the average resale values of houses, and types of housing in the two communities. Even accepting this limited definition of matching, it is not clear if all neighbourhoods in Hamilton were systematically evaluated, or if the investigators were restricted to only certain neighbourhoods suggested by the City.

At the top of page 30, statistics are given concerning the rates of migration out of the exposed and control communities. As the investigators state, these figures make it clear that the proportion of migrators out of the exposed community was much higher. Because migrators probably differ from non-migrators, both sociologically and in ways which may be related to health, this strongly suggests that the communities differ in at least one important respect apart from the exposure per se. Hence matching communities on property resale values has failed to control for the potentially important confounding effect of migration. The investigators have tried to deal with this particular variable in the analysis, but it is disappointing that the sampling design failed to do so for them. [Note: confusing typo on p.30: line 2 should read "time of interview".]

8. Comments on Questionnaire (page 30 and onward).

Careful attention has been paid to the questionnaire design and the quality of the information it produces. Pretesting and trying alternative methods of administration add to its credibility.

On a small point, in item (c) on page 32, can one presume that the residence history was taken for individuals within each household? This would be desirable to allow for certain members of a family to have resided for different lengths of time during the exposure period.

9. Respondent and interviewer knowledge of study objectives.

Potential respondents in both study areas were alerted in their initial contact letter to the reason for the study, i.e. the health effect of the landfill. Such candour may have helped to improve cooperation and response rates, but it may also have had an influence on response patterns. The investigators state that they think some of the controls may actually have considered themselves to be "exposed"; if this is so it would help to reduce any response bias between those truly exposed or unexposed. It would have been very interesting to assess this possibility by examining the data according to the respondents' own perceptions of their own exposure level - for instance comparing controls who did or did not regard themselves as exposed. Unfortunately this was not done, and so the possibility remains that having informed the respondents of the purpose of the study may have unwittingly introduced bias into their answers.

Another problem is the unblinding of the interviewers. It is stated that they were blind to the hypotheses being tested. By this I presume one means the detailed patterns of health effects which were being regarded as main or secondary hypotheses. One has to wonder how realistic this is; given the publicity surrounding the study, and given the fact that some of the interviewers may have worked on the previous workers study, maybe some of them were not blind at all. At the very least, interviewers knew which study group their interviewees belonged to (on the basis of residence), and this alone may have biased the between-group comparison. To be fair, it would have been very difficult to blind the interviewers and maintain some of the other strengths of the design. However I would like to have seen more investigation of the possibility of response bias of the kinds indicated above.

10. Analytic hypotheses (Table 6).

This table outlines the main comparisons to be made in the data. I have just one concern, regarding question (d). To determine if "the landfill area attracts less healthy people", a comparison is made between people who moved into the landfill area since 1980 with controls, of both short and long-term residence.

It would seem to me to have been more appropriate to compare people who have recently (since 1980) moved into the landfill area with people who have recently moved into the control area. The comparison actually made in the Report is confounded by any differences between "movers" and "stayers" in general, regardless of their place(s) of residence. Because of this, I have some difficulty interpreting the analyses carried out on this question.

11. Cox regression analyses (page 39-40).

The coefficients of the Cox model provide estimates of instantaneous hazard rates, not cumulative incidence rates as stated. The proportional hazards assumption, which is the essence of the Cox model, assumes that the instantaneous hazard ratio is constant over time, but arbitrary in shape. It is not clear to me how the cumulative incidence rates have actually been derived.

12. Subanalyses - gradient analysis (page 40-41).

As I indicated earlier, the exposure groups which have been formed are relatively crude, based on ranges of exposure distances and residence times. The investigators state (page 40, lines 8-14) that they did not carry out subgroup analyses organised by duration of exposure, because there is no direct evidence that emissions were constant over 1976-80. By the same token, however, we should recognise that the exposure groups actually used in their analyses are not homogeneous; for instance there will be some variation in duration, distance, and pattern of exposure. This may have

reduced the power of the statistical analysis.

13. Abstraction study (page 50)

The attention paid to the reliability and validity of the medical record abstraction data is a strong point of the study, and might well be used as a model in other investigations. I was particularly impressed by the methods used to establish categories for confirmation of problems, and the workshops held to establish reliability. The only surprise was that the investigators were prepared to hold the data from the first workshop in cold storage until the end of the study, when a second workshop was held. It is fortunate for them that the reliability from the first occasion was as high as it was; if it been lower, it would have cast doubts on the credibility of the whole study.

14. Response rates (page 52)

As the Report acknowledges, the control response rate was much lower than desirable, and this leaves open the possibility of bias between the respondents and non-respondents.

It is a pity that there was no further effort to assess this bias. One way to do this would have been to compare known characteristics of the non-respondents to the respondents, for example on property values, length of residence, and any other relevant variables. Another possibility is to compare respondents who participated "eagerly" (e.g. entered the study willingly after the first contact) or "reluctantly" (e.g. entered the study only after persuasion with follow-up letters, etc.). If these groups not shown any important differences, one would have felt less concerned about the volunteer bias effect. As it stands, one can only speculate how serious this problem might be.

15. Comparability of exposed and control regions. (page 52 and onward).

As I have indicated earlier, comparability of the exposed and control region is crucial to the interpretation of this study. From the data provided, I have to conclude that the control region chosen is far from ideal, and it appears to differ from the landfill area in a number of important respects.

Of particular concern are the differences indicated in educational levels, age, smoking and alcohol consumption, current occupation, and percentage of homeowners. Persons in the exposed areas had a lower educational attainment levels, were younger at first residence, included more current smokers, and included less homeowners than among the controls. All of these factors may be associated with health in a variety of ways, and so may act as confounders.

The differences in the percentage of homeowners is partially explicable by the Ontario Housing Corporation plan to sell more houses in the landfill area at a reduced price and for rental. Even despite this artifact, one still has to be concerned that persons attracted to housing of this type are going to differ substantially from persons who elect to buy their homes outright in another area.

To their credit, the investigators have tried to deal with at least some of these difference by control in the statistical analysis. This is only a partial solution, however, as it is unlikely that all the effects which these confounders represent are adequately represented by summary variables as used in the multivariate regression analyses. Even using a complex and sophisticated statistical analysis, the substantial differences between exposed and control communities must remain a major concern in the validity of the conclusions from this study.

16. Adjustment for confounding in main analyses (page 63).

Given my concerns about non-comparability of the study regions, I hoped that thorough control of confounders would be exercised in the multivariate analyses. Confounders which were made available and allowed to enter the multivariate models are given in Table 15.

I was unclear why, for instance, "ever smoked daily" was selected as the only smoking variable in preference to "current smoker", "amount smoked per day" or several other possibilities. This is a great concern especially in the analysis of respiratory conditions, where very tight control of smoking differences should have been attained before examining the effect of landfill exposure.

A more general concern is that confounders were introduced into the multivariate regression models only if they attained a certain level of statistical significance. A number of papers and monographs in the epidemiologic literature have shown that this is often a poor strategy. Basically, the problem is that relatively small (and statistically non-significant) differences between comparison groups (in this study the exposed and unexposed) in certain variables (e.g. smoking) may correspond to important differences in the outcomes under investigation. This will happen when these variables are strong determinants of the outcome, as is so for smoking and respiratory symptoms.

As it turned out, the "ever smoked daily" variable did not enter the multivariate analysis of respiratory conditions. The exposed/unexposed comparison therefore remains unadjusted for smoking in any way. Because there are more smokers in the exposed region, part of the landfill effect as quoted in Table 14 may in fact be due to smoking. I am very unhappy about accepting the relative risks and other conclusions of the analyses in Table 14 (and similarly elsewhere) when a known and important risk factor has been

neglected in this way.

More generally, I am not satisfied that potential confounders which are known risk factors for any of the conditions have been adequately controlled. Such factors should be forced into the model, and the effect of the landfill exposure then examined conditionally on the inclusion of these other factors in the model. Until this is done, there is the strong possibility that the associations with landfill exposure found in the data will have been distorted. Such distortion could have been in either direction, i.e. either to increase or decrease the relative risk of exposure.

17. Gradient analysis (page 67)

Dose-response is assessed by comparing "very near exposed", "near exposed" and control districts. Specifically, trend or gradient is tested using linear coding, i.e. scoring these districts 2,1, and 0 or similarly. This assumes "equal stepping", i.e. that the difference in health risk between the two exposed areas is the same as the difference between the further exposed region and the controls. This may not be reasonable, and indeed the data of Table 16 indicate clearly that this pattern did not occur always. For instance, "combined skin" shows a very non-linear pattern. As I have suggested earlier, it might have been better here to use exact residence distances instead. However, using the three broad exposure groups, the analysis here would have been enhanced by a formal test for non-linearity. Another improvement would have been a statement of the gradient "slope" coefficients, which would have indicated the magnitude of the dose-response relationship in addition to its statistical significance.

The finding that there are strong linear trends for long-term residents, but not for persons who spent less than 3 years during the

dumping period, is especially good evidence of an effect. This conclusion is reached mainly on the basis of the associated significance tests. But again it would have been useful to see the slope coefficients. The number of health events among short term residents is much smaller, and so the non-significance of the gradient analyses for this group could be because of lower statistical power.

18. Migrator bias (Page 81 and nearby)

Various comparisons of migrator and non-migrator individuals are made, counting either all events or only events in 1980 or before. Some of the relevant relative risks (migrators vs. non migrators) are as follows (from Tables 25, 23 and 19).

	<u>Respiratory</u>	<u>Skin</u>	<u>Narcotic</u>	<u>Mood</u>	<u>Red eyes</u>
All events	0.72	0.92	1.04	1.08	0.82
Events before 1981	1.22	1.05	1.25	1.56	0.94

Comparisons of these figures is difficult because they come from both exposed and unexposed groups combined. As we have seen, substantial differences between the two regions exist with respect to migration rates, and so migration is confounded with exposure. Comparisons of the first and second row of the above table are also complicated by the fact that the first includes the second; it would have been better to compare events before and after 1981 as separate categories.

These concerns aside, the above relative risks suggest, for instance, that migrators had more respiratory conditions before 1981 but less afterwards, in relation to controls. It is possible that at least some persons migrated because of their condition, i.e. to remove themselves to another environment.

In the Report, tests of the above relative risks are against a null

value of 1.0. More relevant to the examination of migrator bias would be a test of interaction in the data before and after 1981, i.e. to examine if the change in relative risk is significant. This should be done for exposed and unexposed groups separately to eliminate the confounding of migration and exposure. As it stands now, I cannot necessarily agree with the investigators' conclusion that migrator bias is unimportant.

19. Conditions thought not to be related to exposure (page 83 and onward)

By and large the analyses of these conditions (Table 28) show no effect. The only exceptions were loss of weight, loss of appetite, and burns. As the Report says, this may be a true effect, but it may also be a chance finding, despite the attempts to deal with the problem of multiple significance tests.

I would tend to regard the mostly negative results of Table 28 as indicating no significant level of reporting bias between the exposed and unexposed regions.

20. Gradient analyses for child data (page 92).

The investigators argue that these analyses "are less valid for children than for adults", because children spend a substantial amount of time at school, making residence a poor predictor of exposure. If this is accepted, then one should also recognise that some of the adult sample spend substantial amounts of time away from home, and so residence may be a poor marker variable for them also.

Offhand, I would not accept that one gradient analysis is any more or less valid than the other. Better control of personal lifestyle variables may have been able to deal with this question.

21. Pregnancy data (page 113).

A minor point, but the year groupings of Table 45 contain different numbers of years. 1976-80 contains 5 years whereas the other two groups only

contain 4 years. However, even adjusting for this, it is still true than more births per year took place in the middle time period.

22. Discussion (page 142).

Unfortunately Table 67, the key to this section, appears to be incomplete in my copy of the Report. Otherwise, the Discussion appears to fairly represent and summarise the detailed content of the Report.

3. CONCLUSIONS

The investigators have, as in their previous study of workers at the landfill site, carried out an excellent piece of work on a difficult subject. Many aspects of their approach should serve as models for similar studies elsewhere, and my sometimes negative comments on methodology should not detract from this. This type of investigation is relatively new to epidemiologists, but one which is likely to be needed more often in the future as environmental concerns increase.

Particular problems faced in this study were the vague and interchangeable nature of the health conditions being implicated, the fact that the study began some time after exposure had taken place, and that it took place in an atmosphere of heightened public awareness of the problem. The attention paid to reliability of self-reports through the use of careful medical record abstraction is noteworthy.

Another strength is the pre-specification of primary and secondary hypotheses to be tested, and explicit definitions of criteria for causal inference. This has been done in much greater detail than is usual, and has undoubtedly pre-empted the temptation to follow up on some conditions which were shown to be marginally associated with landfill exposure, which were not previously anticipated, and which probably represent false positive

findings.

Despite these strengths, I find it difficult to support the investigators' findings because of my concerns about certain aspects of the design and analysis. These concerns have been described above in section 2, but they are related mainly to (a) the adequacy of the control region, (b) the method of controlling confounding in the analysis, (c) the possibility of respondent bias, and (d) migration bias.

For the first of these (adequacy of the control region), my impression is that the Gilkson district differs substantially from the landfill area in ways which may be strongly related to health outcomes of many types. Not knowing the detailed practical constraints which would have been imposed on the investigating team, it is hard for me to say if this problem might have been remedied at the design stage.

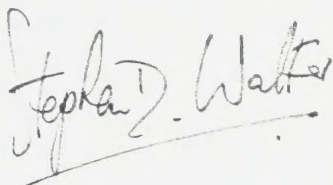
Concerning the treatment of confounding in the analysis, it is possible that further analyses of the existing data set might show that some of my fears about confounding would not materially affect the conclusions, but it is impossible to say for sure with the information provided. The analytic sections of the Report do, however, strongly suggest that residual confounding remains in at least some of the exposed-unexposed comparisons which are described.

My detailed concerns about the possibility of non-response bias (especially in the control group) and migration bias are given in section 2. Both of these may have had a sizeable influence on the conclusions.

With these concerns, at this point I could not strongly support further study of this population, at least in the level of detail as used thus far. I think it would be reasonable to monitor the cancer incidence of the landfill-exposed group; this could be done at relatively modest expense,

through the Ontario cancer registry of the Ontario Cancer Foundation, and would allow an examination of one of the potential longer term effects of exposure, as opposed to the mainly short-term effects described in the bulk of the Report. Another relatively inexpensive possibility would be a continuing mortality study of the group, using vital statistics. Both of these approaches could compare the health experience of the landfill-exposed group to all or appropriate parts of the rest of Ontario, thus avoiding many of the bias problems which exist in the Gilkson comparisons.

Beyond such study of "hard" health outcomes, one would have to consider follow-up investigations such as of the psycho-social state of the exposed and control groups, or of pulmonary function and behavioural testing. This type of investigation would, by virtue of its labour-intensive nature, be expensive; it is also likely to suffer from the same difficulties of interpretation as the present study. Given the uncertainties which exist in the conclusions from the data already collected, I could not support the allocation of substantial additional funds for this purpose.

A handwritten signature in dark ink, reading "Stephen D. Walter". The signature is written in a cursive style with a horizontal line underneath the name.

S.D.WALTER, Ph.D.

Hamilton, Ontario.

ACCOPRESS®

25071	—	BLACK / NOIR	—	BG2507
25072	—	BLUE / BLEU	—	BU2507
25078	—	RED / ROUGE	—	BF2507
25075	—	GREEN / VERT	—	BP2507
25074	—	GREY / GRIS	—	BD2507
25073	—	R. BLUE / BLEU R.	—	BB2507
25079	—	X. RED / ROUGE X.	—	BX2507
25070	—	YELLOW / JAUNE	—	BY2507
25077	—	TANGERINE	—	BA2507

ACCO CANADIAN COMPANY LIMITED
COMPAGNIE CANADIENNE ACCO LIMITÉE
TORONTO CANADA

HAMILTON PUBLIC LIBRARY



3 2022 21333708 8